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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/466,325	12/17/99	BRISCOE	C 99.305

IM22/0801

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EXAMINER	
SINES,B	
ART UNIT	PAPER NUMBER
1743	8

DATE MAILED: 08/01/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)
	09/466,325	BRISCOE ET AL.
	Examin r	Art Unit
	Brian J. Sines	1743

-- The MAILING DATE of this communication appears on th cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Drawings

The drawings are objected to under 37 CFR 1.83(a). The drawings must show every feature of the invention specified in the claims. Therefore, with regards to claims 24 and 25, the means for delivering reagents must be shown or the feature(s) canceled from the claim(s). No new matter should be entered.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1 – 32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

With regards to claim 1, it is unclear as to how each of the elements of the apparatus are structurally connected to one another. How are the well structures connected to the supporting substrate? How is the thermal conducting layer separated by a thermal insulating layer? With regards to claims 5 and 9, it is unclear as to what structural limitations are imparted to the apparatus by using ceramic multilayer technology. With regards to claim 5, it should be noted that this claim specifies a process of making the apparatus, i.e., using ceramic multilayer technology. Claim 5 is a process claim which is dependent upon claim 1, which claims the structure of the apparatus. The process limitations specified in claim 5 are accorded no patentable weight in the claims for an apparatus. As the structure of the apparatus as suggested

by the combined teachings of Hayes et al. in view of Kroy et al. is identical to the apparatus of claim 1, it would appear that the method of making the apparatus would also be the same. Process limitations do not add patentablility to an apparatus structure which is not distinguished from the prior art. Similarly, the process limitations as specified in claim 9 regarding the use of ceramic multilayer technology in fabricating the thermal insulating layer are accorded no patentable weight in the claims for an apparatus.

Claim 25 recites the limitation "means for delivering reagents" in line 25. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1 – 4, 6 – 8, 10, 13, 14, 17 – 26 and 28 – 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hayes et al. (US 5,849,208) in view of Kroy et

al (US 5,252,294). Regarding claim 1, Hayes et al. teach an apparatus 10 comprising: a supporting substrate 20; a plurality of separate well structures 40-42 comprising a thermal conducting layer and wherein the well structures are separated by a thermal insulating layer contained in regions defined by 30a - 30c; a means for heating 50-52 each well structure in thermal contact with the thermal conducting layer comprising each well; a means for cooling 90 each well structure in thermal contact with the thermal conducting layer comprising each well; a means for monitoring the temperature 182 of the contents of each well structure in thermal contact with the thermal conducting layer comprising each well (col. 1, line 1 – col. 16, line 7). Hayes et al. teach a spacer section 58, which is a thermal conducting layer, that electrically insulates the heating element 54 from the contents of the reaction chamber 40, but is thin enough to permit rapid and efficient heat transfer from the heating element 54 to any material contained in the reaction chamber (col. 5, line 62 – col. 6, line 3). Hayes et al. do not teach that the device may be manufactured from a ceramic material. Kroy et al. teach a micromechanical structure, having a plurality of cavities or wells, which is intended for chemical analysis applications (col. 1, lines 1 – 63). Kroy et al. teach that the structure may comprise a ceramic material (col. 10, lines 33 – 55). Furthermore, ceramics are known corrosion resistant and heat-resistant, or thermally nonconductive, insulative materials. Therefore, it would have been obvious to manufacture the supporting substrate from a ceramic material and to incorporate this ceramic material as a thermally insulating layer between each of the wells, since the courts have held that the selection of a known material based upon the suitability of the material for the intended

use is within the ambit of one of ordinary skill in the art [In re Leshin, 125 USPQ 416 (CCPA 1960)]. The motivation to use a ceramic material in the fabrication of the apparatus taught by Hayes et al. would have been to facilitate effective thermal isolation of each of the wells, since each of the wells may be independently controlled using different temperature cycles.

Regarding claim 2, Hayes et al. teach that the apparatus may be especially useful for performing and analyzing the results of a polymerase chain reaction (PCR) (see Abstract).

Regarding claim 3, Hayes et al. teach that the chambers are spaced from each other a distance 30c as illustrated in figure 1. The substrate material in spaces 30a-30c maintains the structural integrity of the substrate 20 around the reaction chambers 40-42 and also provides clearances for controllable heaters 50-52 (col. 4, lines31 – 36). Since Hayes et al. teach that each of the reaction chambers may be independently temperature controlled, it is deemed reasonable that one of ordinary skill in the art would have contemplated the incorporation of a thermally insulating material within these regions, and therefore institute the fabrication of the entire supporting substrate 20 using this thermally insulating material (col. 5, lines 38-50). The motivation to use a thermally insulating material for the fabrication of the supporting substrate would have been to effectively thermally isolate each of the reaction chambers from one another in order to provide effective temperature cycling control. Therefore, it would have been obvious to manufacture the supporting substrate of the device from a thermally insulating material.

Regarding claim 4, Hayes et al. teach that the supporting substrate may comprise polyimide (col. 7, lines 46 - 50). Polyimide is a polymer material, and therefore a plastic material. Polyimide is classified as any group of high polymers containing an imide group in the polymer chain; characterized by high tensile strength, high temperature stability, and resistance to friction, wear, and radiation. Hayes et al recognizes the benefits and suitability, e.g., temperature stability, of utilizing a polymer material, such as polyimide, in the fabrication of the supporting substrate of an apparatus used in chemical analysis, such as PCR. Therefore, it would have been obvious to fabricate the thermal insulating material from a plastic material, including other materials such as glass, silicon or ceramic, since the courts have held that the selection of a known material based upon its suitability for the intended use is within the ambit of one of ordinary skill in the art [In re Leshin, 125 USPQ 416 (CCPA 1960)].

Regarding claims 6 and 13, Hayes et al. teach a spacer section 58, which is a thermal conducting layer, that electrically insulates the resistive heating element 54 from the contents of the reaction chamber 40, but is thin enough to permit rapid and efficient heat transfer from the heating element 54 to any material contained in the reaction chamber or well structures (col. 5, line 28 – col. 6, line 3). The thermal conducting layer 58 contains, or holds within a limit, the resistive heating element 54. The motivation to incorporate a thermal conducting layer containing an integrated resistive heater would have been to provide for effective temperature control for each of the well structures. Therefore, it would have been obvious to incorporate a thermal conducting

layer, which contains, or has within an integrated resistive heater, with the well structures in the apparatus.

Regarding claim 7, Hayes et al. teach that the well structures, or reaction chambers 40-42, are partially formed from a spacer section 58, which is a thermal conducting layer, that electrically insulates the resistive heating element 54 from the contents of the reaction chamber 40, but is thin enough to permit rapid and efficient heat transfer from the heating element 54 to any material contained in the reaction chamber or well structures (col. 5, line 28 – col. 6, line 3).

Regarding claim 8, Hayes et al. teach that the supporting substrate 20 may comprise polyimide (col. 7, lines 46 - 50). The substrate material is also the same material incorporated in the material within the region defined by 30a-30c separating the well structures as shown in figure 1. Polyimide is a polymer material, and therefore a plastic material. Polyimide is classified as any group of high polymers containing an imide group in the polymer chain; characterized by high tensile strength, high temperature stability, and resistance to friction, wear, and radiation. Hayes et al recognizes the benefits and suitability, e.g., temperature stability, of utilizing a polymer material, such as polyimide, in the fabrication of the supporting substrate of an apparatus used in chemical analysis, such as PCR. Furthermore, ceramics are known corrosion resistant and heat-resistant, or thermally nonconductive, insulative materials. The motivation to use a ceramic material in the fabrication of a thermal insulating layer would have been to effectively thermally isolate each well structure in order to facilitate efficient independent temperature cycling control for each well. Therefore, it would have

been obvious to incorporate a thermal insulating material made from a plastic material, including other materials such as glass, silicon or ceramic, since the courts have held that the selection of a known material based upon its suitability for the intended use is within the ambit of one of ordinary skill in the art [In re Leshin, 125 USPQ 416 (CCPA 1960)].

Regarding claim 10, copper is a known material, which is capable of electrically insulating the resistive heating element 54. Hayes et al. teach that the resistive heating element may be formed from any of a variety of electrically resistive and therefore thermally conductive materials, such as nickel/chromium alloys, suitably doped semiconductors, etc. (col. 5, lines 51 – 61). The motivation to use either copper, or a nickel alloy, as a thermal conducting material in the fabrication of the well structures would have been to facilitate effective heat transfer and temperature control for the apparatus. Therefore, it would have been obvious to utilize either undoped silicon, modified plastics, silver, silver palladium, copper, nickel-molybdenum, platinum, or gold as the thermal conducting material since the courts have held that the selection of a known material based upon its suitability for the intended use is within the ambit of one of ordinary skill in the art [In re Leshin, 125 USPQ 416 (CCPA 1960)].

Regarding claim 14, Hayes et al. teach that controllable resistance heater 50, which is shown in greater detail in figure 2 and illustrative of heaters 50-52, is integrally formed within the substrate. Hayes et al. teach that any heater having a heating element in thermal contact with a reaction chamber is suitable (col. 5, lines 29 – 36). Temperature control within these microfluidic devices are generally supplied by thin film

resistive heaters. The motivation to incorporate a thin film resistive heater within the integrated heating system would have been to facilitate the effective temperature control for the reaction wells using a proven and suitable heating means well known in the art. Therefore, it would have been obvious to incorporate an integrated heating system which incorporates a thin film resistive heater.

Regarding claims 17 and 18, Hayes et al. teach that the apparatus is controlled using a programmable controller (col. 14, line 5 – col. 16, line 7). One of ordinary skill in the art would have contemplated a row and column addressing or an individual electrical addressing system in order to keep record of the status of each of the reaction wells of the structure during analysis. The motivation to use either a column and row addressing system or an individual addressing system would have been to effectively monitor and control each of the reaction wells during the temperature cycling process. Therefore, it would have been obvious to incorporate an integrated heating system which utilizes either column and row addressing or individual electrical addressing.

Regarding claims 19 – 22, Hayes et al. teach a heat sink 90 is secured to the second major face 24 with a thermally conductive adhesive 92. The heat sink may either be a conventional thermo-electric device, which is an active cooling system, or have a finned surface, which is a passive cooling system, or both. Hayes et al teach the use of thermo-electric coolers (col. 4, line 63 – col. 5, line 4). The motivation to incorporate an integrated cooling system within the apparatus would have been to facilitate effective temperature cycling control for the reaction wells using a proven and

suitable cooling means well known in the art. Therefore, it would have been obvious to incorporate an integrated passive or active cooling system for each well. Furthermore, it would have been obvious for one of ordinary skill in the art to incorporate an integrated cooling system, which comprises either a metal plate, an array of metal discs, or a thermo-electric cooler in thermal contant with each of the well structures of the apparatus.

Regarding claims 24 and 25, Hayes et al. teach a microfluidic dispensing means for delivering reagents into each well structure (col. 11, lines 42 – 64).

Regarding claims 26 and 28, Hayes et al. teach that the well structures may be sealed (col. 12, lines 47 – 62). The motivation to incorporate sealed well structures with the apparatus would have been to prevent any of the reagents from evaporating. Therefore, it would have been obvious to incorporate sealed well structures using a cover into the apparatus.

Regarding claims 29 and 30, Hayes et al. teach that heater 154 may assume any geometry which places it in thermal contact with the reaction chamber (col. 9, lines 5- 23). Hayes et al. also teach that a thermo-electric heater can be incorporated directly into the substrate (col. 10, lines 13 – 19). The motivation to incorporate a cover which further comprises a heating means for heating the well structures would have been to facilitate effective temperature control for the device. Therefore, it would have been obvious to incorporate a cover further comprising an integrated heating means for effectively heating the well structures of the apparatus.

Regarding claims 31 and 32, Hayes et al. teach the use of wire thermocouples and thin film thermocouples for temperature sensing. Thin film thermocouples may comprise a separate layer within the substrate 120. Thin film thermocouples may also be incorporated into portions of a polyimide layer (col. 5, lines 59 – 61; col. 8, lines 60 – 65). The motivation to incorporate a means for monitoring the contents of each of the well structures would have been to facilitate effective temperature sensing. Therefore, it would have been obvious to incorporate a means for monitoring the temperature of the contents of each well structure which is a resistive thermal detector, or a thermocouple, which can be molded into the plastic of the apparatus.

Claims 11 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hayes et al. in view of Kroy et al. as applied to claims 1 – 4, 6 – 8, 10, 13, 14, 17 – 26 and 28 – 32 above, and further in view of Anderson et al. (US 6,168,948 B1). Hayes et al. and Kroy et al. do not teach the use of parylene as a coating compound. Anderson et al. do teach the coating of surfaces with parylene (col. 20, lines 27 – 44). The motivation to use parylene as a coating compound would have been to provide a non-stick coating for the system to prevent the adhesion of the components of the molecular reaction with the system components. Therefore, it would have been obvious to use parylene as a coating for the thermal insulating, or conducting materials, comprising the well structures of the apparatus.

Claims 15 and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hayes et al. and Kroy et al. as applied to claims 1 – 4, 6 – 8, 10, 13, 14, 17 – 26

and 28 – 32 above, and further in view of Burns et al. (US 6,057,149). Hayes et al. and Kroy et al do not specifically teach the use of a metal wire resistive heater, which is integrated into the thermal insulating material comprising the supporting substrate of the device. Metal wire resistive heating elements are generally well known in the art. The motivation to incorporate a metal wire resistive heater within the integrated heating system would have been to facilitate the effective temperature control for the reaction wells using a proven and suitable heating means well known in the art. Therefore, it would have been obvious to incorporate a metal wire resistive heater within the integrated heating system. Furthermore, regarding claim 16, Hayes teach that the heating elements are formed integrally with the substrate (col. 13, lines 1 –4). The motivation to integrate the metal wire resistive heater into the thermal insulating material comprising the supporting substrate would have been to facilitate the effective temperature control for the reaction wells using a proven and suitable heating means well known in the art. Therefore, it would have been obvious to integrate a metal wire resistive heater into the thermal insulating material comprising the supporting substrate.

Claim 23 is rejected under 35 U.S.C. 103(a) as being unpatentable over Hayes et al. in view of Kroy et al. as applied to claims 1 – 4, 6 – 8, 10, 13, 14, 17 – 26 and 28 – 32 above, and further in view of Kellogg et al. (US 6,063,589). Hayes et al. do teach the use of a thermocouple wire and a thin film thermocouple wire for temperature sensing (col. 8, lines 40 – 65). Hayes et al. and Kroy et al. do not teach the use of an integrated optical or electrochemical sensor system for temperature sensing. Kellogg et al. do teach the use resistive heaters as thermosensors, which utilize screen-printed

positive temperature coefficient (PTC) inks, for temperature sensing within a microfluidic apparatus (col. 56, lines 34 – 63). The motivation to incorporate an electrochemical temperature sensing system would have been to facilitate the effective temperature measurement and control for the reaction wells using a proven and suitable sensing means well known in the art. Therefore, it would have been obvious to incorporate a means for monitoring the temperature of the molecular interactions in each well structure which is either an electrochemical or an integrated optical system.

Claim 27 is rejected under 35 U.S.C. 103(a) as being unpatentable over Hayes et al. in view of Kroy et al. as applied to claims 1 – 4, 6 – 8, 10, 13, 14, 17 – 26 and 28 – 32 above, and further in view of Anderson et al. (US 6,168,948 B1). Hayes et al. and Kroy et al. do not teach that the well structures are sealed using a layer of mineral oil. Anderson et al. do teach the use of mineral oil deposited over the reaction chambers of a microfluidic device as a sealing means. The motivation to use mineral oil as a sealing means for the well structures would have been to prevent excessive evaporation of the sample while allowing the evolution of gas evolution during analysis. Therefore, it would have been obvious to incorporate a mineral oil layer as a means of sealing the well structures of the apparatus.

Prior Art

The prior art made of record and not relied upon is considered pertinent to the applicant's disclosure: The prior art teaches various microfluidic devices.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian J. Sines whose telephone number is (703) 305-0401. The examiner can normally be reached on Monday - Friday (11:30 AM - 8 PM EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill A. Warden can be reached on (703) 308-4037. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-7719 for regular communications and (703) 305-7719 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0661.

BJS
July 24, 2001

Jill Warden
Jill Warden
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